AD_____

Award Number: W81XWH-05-1-0266

TITLE: Cord Blood Stem Cell Procurement in Minority Donors

PRINCIPAL INVESTIGATOR: Voravit Ratanatharathorn, M.D.

CONTRACTING ORGANIZATION: Wayne State University
Detroit, MI 48202

REPORT DATE: March 2007

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01-03-2007	Annual	1 Feb 2006 – 31 Jan 2007

4. TITLE AND SUBTITLE

Cord Blood Stem Cell Procurement in Minority Donors

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-05-1-0266

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Voravit Ratanatharathorn, M.D.

Email: ratanath@karmanos.org

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Wayne State University
Detroit, MI 48202

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES
Original contains colored plates: ALL DTIC reproductions will be in black and white.

14. ABSTRACT

This progress report summarizes the clinical activity of cord blood procurement and the preliminary analysis of the yield of cord blood cells for the purpose of clinical transplantation. The purpose of collection and procurement of cord blood is for public use and will be accessible to all stem cell transplantation centers worldwide. Cord blood is a readily available source of hematopoietic stem cells. It is more accessible than other sources such as live donors, since the cryopreserved cord blood units (CBU) have already been extensively characterized in terms of tissue typing and screening for infectious disease markers. The CBU from minority donors, especially African/American, is particularly valuable because of the difficulty with finding a matched donor. The CBU allows for less stringent matching; thus, CBU is a rapid solution to patients who are in urgent need of stem cell transplantation and have no living donor available. We will now summarize the findings of our efforts to expand the cord blood collection program in an outreach setting with a comprehensive educational program to recruit African/American donors. We are able to demonstrate a significant increase of the CBUs collected with time indicating improvement of access to the African/American donor. This activity may compensate for the poor individual yield of the total nucleated cells in the African/American donor CBU and therefore, prove to be a more effective method to build the CBU inventory.

15. SUBJECT TERMS
cord blood, transplantation, minority, African/American, stem cell, donor

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	10	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

Introduction…….……....Page 4

Body…….…….Page 4

Key Research Accomplishments…….……Page 9

Reportable Outcomes…….…….Page 10

Conclusions…….……..Page 10

INTRODUCTION

The main purpose of this research project is to increase the efficiency of procurement of minority cord blood units for clinical stem cell transplantation. The outcome of the first year of this project revealed several key findings:

- CBUs harvested from African/American mothers using *in utero* technique contained lower total nucleated cells than Caucasian mothers.
- There was no correlation of the cell yield with gravida, prenatal clinic visit and health variables.

At the end of the first year of this project, we concluded that improvement of the prenatal clinic visit is not likely to increase the numbers of usable cord blood units (CBUs) for clinical stem cell transplantation. This study suggested that improvement of quality of CBUs may have to be compensated by improvement of access to the collection sites and that expansion of the collection sites will be the most efficient process.

BODY

A. Strategy to Expand the Collection of African American CBUs

In the second year of this project, we focus our data evaluation with the activity at the St. John Hospital collection site. The J.P. McCarthy Cord Blood Program began collection facility affiliation with St John Hospital and Medical Center in June 2005. The concept of cord blood collection was proposed and adopted by the obstetric staff at St John Hospital; over the past year there are over 40 obstetricians participating in the cord blood collection on their patients upon delivery. Also at the end of last year, we slowly began to collect cord blood in two other hospitals in the metropolitan Detroit area – Detroit Riverview Hospital and Providence Hospital. The latter two sites have a lower collection activity due to limited human resources to expand to full collection capacity. The development process of the standard operating procedures for cord blood collection has been modeled for adoption to additional collection sites. The collection technique of cord blood units at St. John's Hospital is 'in utero' in order to optimize the yield and reduce contamination of the CBUs. While the demographics at the St. John site is mainly Caucasian mothers (with a growing number of African American mothers), the collection sites at Detroit Riverview Hospital and Providence Hospital is mostly African American. The projection of the available units for collection and banking are shown below.

Metro Area Expansion Opportunities for Minority Units

Hospital	2006 Births* (est.)	2006 collections (est.)	2006 Units banked (est.)	2007 collection (est.)	2007 Units Banked (est.)	Banked collections
St. John Detroit	3600	1200	385	1440	460	32%
St. John Riverview	1340			400	128	
St. John Providence	3400			1100	352	

*information obtained from the Beaumont Survey

In order to improve the collection of the African/American CBUs, we initiated an educational program to reach the minority community. A comprehensive Cord Blood Program of education has also been formulated and some of the components of this program were implemented in 2006. We target three main population groups with this educational program:

1. Community-wide education in the geographical areas with a high population of African/Americans. The targeted geographical areas in the City of Detroit according to 2004 survey is shown below:

Live Births to Mothers 18-35 by race of Mother, Detroit City Residents, 2004

Zip Code	White	Black	American Indian	Asian/Pacific Islander	Other	Unknown	Total
48214	8	285	1	2	0	0	296
48215	10	242	1	0	0	0	253
48207	15	234	0	0	1	2	252
48213	9	548	0	2	0	3	562

We also created a website for public education dedicated to the Cord Blood Program - www.karmanos.org/cordblood/

2. Information sessions, education to the individual birth care providers in the community, outreach to health care providers and social service agencies serving pregnant and childbearing age black women is an important component of the program. Preliminary work assessing provider and agency awareness has been undertaken. Results of our preliminary work indicates that more than 80% of all healthcare providers (OB/Gyn, Pediatricians, Nurse Practitioners and Physician Assistants) and 95% of all agencies surveyed that serve pregnant or childbearing age black women report being unaware of the J.P. McCarthy Cord Blood Bank, the services it provides, hospitals participating in the Cord Blood Bank and the importance of minority cord blood donation. This component of the program to reach the pediatricians and medical assistants and staff nurses are a part of our broad based approach to education and outreach. This approach will be used to reach as many African/American women of childbearing age as possible.

3. Approach the leadership in the community hospital to buy into the cord blood collection program for the community. The first target is St. John Hospital. Other hospitals to follow are Providence Hospital and Detroit Riverview Hospital. We also plan to send the message to the grass-root level via broadcasting media and community-access cable channels.

The long-range plan for the community outreach program is to improve the cord blood collection by establishing a 'COMMUNITY ADVISORY COUNCIL FOR MINORITY CORD BLOOD DONATION' in Southeastern Michigan. The goal of this advisory council is to develop and implement a Community Advisory Council to address the educational and outreach barriers related to umbilical cord blood donation. Cord blood donation is not a familiar concept to African American women in Metropolitan Detroit. Most women are familiar with the private cord blood banks that require an annual fee to maintain the donated specimen for personal use. There may be questions and concerns and/or organizational barriers that the community has or may have that the Community Advisory Council can assist the Cord Blood Bank to address in the most appropriate manner. The mission of the Council will be to serve the cord blood collection effort by:

- Being cord blood advocates
- Assisting the project by referring the project to agencies and providers
- Providing input on the development and distribution of public service announcements, the educational presentation, materials and organizing meetings.
- To design and produce a culturally relevant minority cord blood awareness education program.
- To design and produce educational materials that support the education program and that can be distributed to health and social service agencies for the community.

B. Measurement of the Impact of Expansion of Cord Blood Collection

At the end of the first year of this project, we concluded that the only maternal variable associated with total nucleated cell yield is maternal race. African American donors had a lower nucleated cell yield and there was no correlation with the frequency of the prenatal clinic visit. Therefore the only practical solution to increase the size of inventory for the African/American cord blood units is to increase the cord blood donation. In 2006, we implemented the recruitment educational program as outlined above. We participated in an educational forum for African/Americans at the Charles Wright African American Museum in Detroit under the leadership of Congresswoman Carolyn Cheek-Kilpatrick in March 2006. The educational pamphlets and other materials produced by the National Marrow Donor Program were used in various meetings of church groups, labor unions and Health-O-Rama. The most important effort was the direct approach by the Principal Investigator and his team members on all the leaders of birth care providers in Southeastern Michigan. Approximately 35% of the birth-care institutions agreed to participate in cord blood collections but it soon became apparent that there was no long-term commitment for this effort. Therefore, the measurement for the second year of this project is focused on the quantity and quality of the units as measured by cell counts, the race of the mothers, and the number of units passing quality control to be used for clinical transplantation. The study group is the CBUs collected at St John Health System from 2/8/06 to 1/31/07.

During the period defined in the study as approved by the IRB, we have collected 1135 CBUs.

1. Expansion of collection to the affiliated sites and the education program increased the total number of CBUs collected

Table 1. Cumulative CBUs Collected

Month/Year	Frequency	Percent	Valid Percent	Cumulative Percent
FEB 06	40	3.5	3.5	3.5
MAR 06	14	1.2	1.2	4.8
APR 06	72	6.3	6.3	11.1
MAY 06	111	9.8	9.8	20.9
JUN 06	112	9.9	9.9	30.7
JUL 06	120	10.6	10.6	41.3
AUG 06	96	8.5	8.5	49.8
SEP 06	106	9.3	9.3	59.1
OCT 06	86	7.6	7.6	66.7
NOV 06	112	9.9	9.9	76.6
DEC 06	120	10.6	10.6	87.1
JAN 07	146	12.9	12.9	100.0
Total	1135	100.0	100.0	

Out of the total of 1135 CBUs collected, there were 52 CBUs from minority racial groups other than African American; these units were from mothers of Asian, Native American, Continental Indian and mixed racial groups. We excluded these 52 CBUs from this analysis.

2. Increased collection of CBUs gradually skewed towards African American CBUs indicating effective penetration of the message into the African American community.

The distribution of African American (Black) CBUs and Caucasian (White) units along the timeline is shown in Table 2.

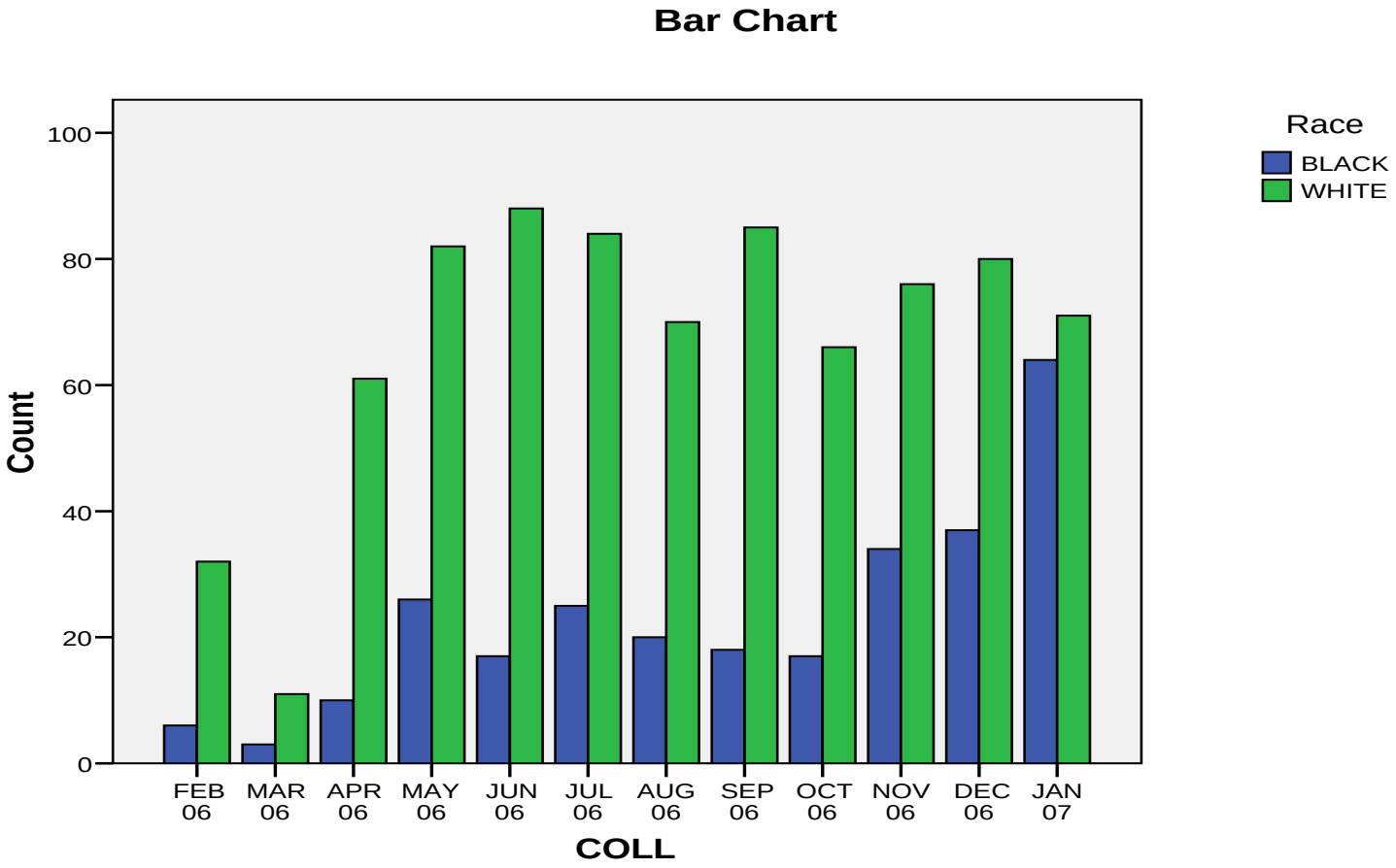
Table 2. Distribution of CBUs Collected During Months of Study

			Race of Mother		Total
			BLACK	WHITE	
Month/Yr	FEB 06	Count	6	32	38
		% within MONTH	15.8%	84.2%	100.0%
		% within RACE	2.2%	4.0%	3.5%
	MAR 06	Count	3	11	14
		% within MONTH	21.4%	78.6%	100.0%
		% within RACE	1.1%	1.4%	1.3%
	APR 06	Count	10	61	71
		% within MONTH	14.1%	85.9%	100.0%
		% within RACE	3.6%	7.6%	6.6%
	MAY 06	Count	26	82	108
		% within MONTH	24.1%	75.9%	100.0%
		% within RACE	9.4%	10.2%	10.0%
	JUN 06	Count	17	88	105
		% within MONTH	16.2%	83.8%	100.0%
		% within RACE	6.1%	10.9%	9.7%
	JUL 06	Count	25	84	109
		% within MONTH	22.9%	77.1%	100.0%
		% within RACE	9.0%	10.4%	10.1%
	AUG 06	Count	20	70	90
		% within MONTH	22.2%	77.8%	100.0%
		% within RACE	7.2%	8.7%	8.3%
	SEP 06	Count	18	85	103
		% within MONTH	17.5%	82.5%	100.0%
		% within RACE	6.5%	10.5%	9.5%
	OCT 06	Count	17	66	83
		% within MONTH	20.5%	79.5%	100.0%
		% within RACE	6.1%	8.2%	7.7%
	NOV 06	Count	34	76	110
		% within MONTH	30.9%	69.1%	100.0%
		% within RACE	12.3%	9.4%	10.2%
	DEC 06	Count	37	80	117
		% within MONTH	31.6%	68.4%	100.0%
		% within RACE	13.4%	9.9%	10.8%
	JAN 07	Count	64	71	135
		% within MONTH	47.4%	52.6%	100.0%
		% within RACE	23.1%	8.8%	12.5%
Total		Count	277	806	1083
		% within MONTH	25.6%	74.4%	100.0%
		% within RACE	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	55.257(a)	11	.000
Likelihood Ratio	52.733	11	.000
N of Valid Cases	1083		

1 cell (4.2%) has expected count less than 5. The minimum expected count is 3.58.



The data shown above shows increasing numbers of CBUs collected and the increase is more pronounced among African/American than the Caucasian counterpart.

3. The volume of CBUs is smaller in African/American units than in Caucasian units but there was no difference in the cell count if corrected for the volume.

Out of 1080 CBUs collected from African/American and Caucasians mothers, (3 units had no measurement of volume and were excluded) the mean volume of the CBUs from African/American mothers and Caucasian mothers were 55.25 and 65.77 mL per unit, respectively. According to the IND used in the cord blood collection, cord blood units with a volume less than 50 ml were excluded. Therefore, the remaining 562 CBUs from Caucasian mothers and 152 CBUs from African American mothers were processed, i.e., the nucleated cell counts were obtained. The cell concentration of the Caucasian CBUs and African/American CBUs were comparable, giving a similar cell yield of 122.79×10^7 and 120.34×10^7 nucleated cells per CBU, respectively.

Table 3. Cord Blood Volume and Total Nucleated Cell Count vs. Race

	Race	N	Mean	Std. Deviation	Std. Error Mean
Cord Blood Volume	WHITE	805	65.77	28.544	1.006
	BLACK	275	55.25	24.616	1.484
Total Nucleated Cell (1×10^7)	WHITE	562	122.79	96.038	4.051
	BLACK	152	120.34	158.226	12.834

	t-test for Equality of Means						
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
	Lower	Upper	Lower	Upper	Lower	Upper	Lower
Volume of CBUs	5.453	1078	.000	10.512	1.928	6.730	14.294
Total Nucleated cells	.240	712	.811	2.456	10.253	-17.673	22.586
	.183	182.104	.855	2.456	13.458	-24.097	29.010

KEY RESEARCH ACCOMPLISHMENTS

- In addition to the findings of the lower total nucleated cell counts of CBUs from African/American mothers (see Progress Report for year 2005), we also found that the volume of the CBUs from African/ American mothers have a significantly lower volume. However, the concentration of the nucleated cells in the units larger than 50 ml was equivalent to the Caucasian counterpart.

- The current recruitment approach among African/American donors is effective, yet it is difficult to assign the relative contribution of the recruitment strategy, i.e., direct dissemination of information in various venues in the African/American community, internet access, education and information provided to birth-care providers, or institutional approach. The educational process was difficult and time-consuming and the lag time to realize the increase in collections may take many months. Therefore, it highlights the need for continuous monitoring of the collection activity in the coming years and current strategy to access the donors may need to be adjusted.

- The success of the educational program implemented will have to be scaled up in order to build the momentum of the collections and refine the maternal health variables associated with nucleated cell yield.

REPORTABLE OUTCOMES

See KEY RESEARCH ACCOMPLISHMENT above.

CONCLUSION

Cord blood collection in the African/American community is an extremely difficult effort. The percentage of African/American cord blood inventory in the US is lower than 20% in most Cord Blood Banks. In this project, we have shown the unique problems with technical aspects of cord blood collection such as the lower nucleated cell yield. We also have shown in previous reporting that the lower nucleated cell yield in African/American donors did not appear to be correlated with the frequency of prenatal clinic visits. Therefore, lower nucleated cell count may be an inherent biologic property of the African/American cord blood donor and there may not be an easy solution to improve the yield by improvement of the prenatal clinic visit. In 2006, we implemented an approach to educate the public at the grass-root level, birth-care providers and institutional levels targeting the institutions with a high proportion of African/American mothers. Despite many difficult barriers, we have succeeded, to a limited extent, in collecting a high proportion of African/American CBUs shown with a rising trend. Expansion of collections by educating the public might be an easier and a more cost effective means of increasing the inventory of African/American CBUs.

In the coming year, we will continue to monitor the collection activities at each site. We will also collect transplant outcome data of the cord blood units provided by the JP McCarthy Cord Stem Cell Bank in comparison to cord blood transplant outcomes performed at Karmanos Cancer Institute.